

## PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:

Davies Collison Cave  
Level 15  
1 Nicholson Street  
MELBOURNE VIC 3000

PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT AND  
THE WRITTEN OPINION OF THE INTERNATIONAL  
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

<i>Recd. in 2/9/04</i>	
Applicant's or agent's file reference 12426030-E	Date of mailing (day/month/year) 02 JUL 2004
International application No. PCT/AU2004/000349	FOR FURTHER ACTION See paragraphs 1 and 4 below International filing date (day/month/year) 19 March 2004
Applicant THE MURDOCH INSTITUTE et al	

1.  The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

## Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
1211 Geneva 20, Switzerland, Facsimile No : +41 22 740 14 35

For more detailed instructions, see the notes on the accompanying sheet.

2.  The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3.  With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

## 4. Reminders

Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/AU  AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized officer  LEXIE PRESS Telephone No. (02) 6283 2677
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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 12426030-E	<b>FOR FURTHER ACTION</b>		see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/AU2004/000349	International filing date ( <i>day/month/year</i> ) 19 March 2004	(Earliest) Priority Date ( <i>day/month/year</i> ) 21 March 2003	
Applicant THE MURDOCH INSTITUTE et al			

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b.  With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2.  Certain claims were found unsearchable (See Box No. II).3.  Unity of invention is lacking (See Box No. III).

## 4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

## 5. With regard to the abstract.

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

## 6. With regard to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No.

as suggested by the applicant.

as selected by this Authority, because the applicant failed to suggest a figure.

as selected by this Authority, because this figure better characterizes the invention.

- b.  none of the figures is to be published with the abstract.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2004/000349

**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:

because they relate to subject matter not required to be searched by this Authority, namely:

2.  Claims Nos.: 45-64 in part

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

see extra sheet

3.  Claims Nos.:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No

PCT/AU2004/000349

## A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl.: C12Q 1/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See electronic database

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See electronic database

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPIDS, MEDLINE, CA, BIOSIS: TLR-2, TLR-4, toll like receptor, cirrhosis, hepatocellular carcinoma, HCC, HepC, HepB, HCV, HBV, hepatitis, virus, viral, disease, diagnos?, treat?, prognosis

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Manigold <i>et al.</i> (2003) 'Differential expression of toll-like receptors 2 and 4 in patients with liver cirrhosis' European Journal of Gastroenterology & Hepatology Vol 15(3): 275-282	1, 2, 4, 6, 10-14, 16, 21-24, 26, 28, 32-36, 38, 43-47, 49, 54-64

 Further documents are listed in the continuation of Box C See patent family annex

## \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"E" earlier application or patent but published on or after the international filing date

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"O" document referring to an oral disclosure, use, exhibition or other means

"&amp;" document member of the same patent family

"P" document published prior to the international filing date but later than the priority date claimed

Date of the actual completion of the international search

28 June 2004

Date of mailing of the international search report

02 JUL 2004

Name and mailing address of the ISA/AU

AUSTRALIAN PATENT OFFICE  
PO BOX 200, WODEN ACT 2606, AUSTRALIA  
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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2004/000349

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Manigold <i>et al.</i> (1999) 'Upregulation of toll-like receptor-2 in patients with liver cirrhosis' Hepatology Vol 30(4) Part 2: 434A	1, 2, 4, 6, 10-14, 16, 21-24, 26, 28, 32-36, 38, 43-47, 49, 54-64
X	O'Neill L. (2000) 'The toll/interleukin-1 receptor domain: a molecular switch for inflammation and host defence' Biochemical society Transactions Vol 28(5): 557-563	1,2, 6, 8-14, 19-24, 28, 30-36, 41-46, 52-64
X	WO 2001/36488 A1 (LEIV EIRIKSSON NYFOTEK AS) 25 May 2001 (see in particular page 1, lines 1-6; claims 26 and 30)	1,2, 6, 8-14, 19-24, 28, 30-36, 41-46, 52-64
P, X	Paik <i>et al.</i> (2003) 'Toll-like receptor 4 mediates inflammatory signaling by bacterial lipopolysaccharide in human hepatic stellate cells' Hepatology Vol 37(5): 1043-1055	1,2, 6, 8-14, 19-24, 28, 30-36, 41-46, 52-64
P, X	Riordan <i>et al.</i> (2003) 'Peripheral blood mononuclear cell expression of toll-like receptors and relation to cytokine levels in cirrhosis' Hepatology Vol 37(5): 1154-1164	1,2, 6, 8-14, 19-24, 28, 30-36, 41-46, 52-64
P, X	Riordan <i>et al.</i> (2003) 'Toll-like receptor expression in cirrhosis' Gut Vol 52 No. Suppl. 1: A2	1,2, 6, 8-14, 19-24, 28, 30-36, 41-46, 52-64
P, X	Visvanathan <i>et al.</i> (2003) 'Up-regulation of toll-like receptor expression in chronic hepatitis C: correlation with circulating pro-inflammatory cytokine levels and hepatic necro-inflammatory activity' Gut Vol 52 No. Suppl. 1: A35	1-3, 6, 10-15, 21-25, 28, 32-37, 43-48, 54-64
P, X	Visvanathan <i>et al.</i> (2003) 'Impaired toll-like receptor expression in chronic hepatitis B' Gut Vol 52 No. Suppl. 1: A36	1, 2, 6, 7, 10-14, 18, 21-23, 29, 32-36, 40, 43-47, 51, 54-64

**Supplemental Box**

(To be used when the space in any of Boxes I to VIII is not sufficient)

**Continuation of Box No: II.2**

Present claims 45 to 64 refer to a large number of possible agents and their use. These agents are defined by a desirable property namely, antagonist/agonist or regulator of TLR-2 or TLR-4. The claims cover all substances and compounds having this property, whereas the application does not provide support within the meaning of Article 6 PCT for any specific example of such substances or compounds. Because the claims lack support, no meaningful search encompassing their entire scope is possible.

The Applicant's attention is drawn to the fact that claims relating to inventions in respect of which no International Search has been established need not be the subject of an International Examination.